K092353

510(k) Summary

OCT 29 2009

1. **Company:**

Bio-Rad Laboratories
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Contact: Linda Staswick

Date Summary Prepared: October 22, 2009

2. **Device Name:**

Device Trade Name:	MONOLISA™ Anti-HAV IgM EIA	EVOLIS™ Automated Microplate System
Common Name:	IgM Antibody to Hepatitis A Virus	Automated Laboratory Analyzer
Classification Name:	Hepatitis A Virus (HAV) serological assays	Discrete photometric chemistry analyzer for clinical use
Product Code:	LOL	JJE
Regulation Number:	21 CFR 866.3310	21 CFR 862.2160
Regulatory Class:	Class II	Class I
Panel:	Microbiology	Chemistry

3. **Substantial Equivalence:**

The MONOLISA™ Anti-HAV IgM EIA used with the EVOLIS™ Automated Microplate System is substantially equivalent to the MONOLISA™ Anti-HAV IgM EIA using the manual method (k063319)

4. **Description of the Device:**

The MONOLISA™ Anti-HAV IgM EIA is an enzyme immunoassay (IgM antibody capture format) for the detection of IgM antibodies to hepatitis A virus. In the assay procedure, patient specimens, a calibrator, and controls are incubated with anti-human IgM antibodies coated on the microwells. If IgM antibodies to HAV are present in a specimen or control, they bind to the antibody. Excess sample is removed by a wash step. The HAV Viral Antigen and the Conjugate (containing horseradish peroxidase - labeled mouse monoclonal antibody to HAV) are successively added to the microwells and allowed to incubate. The presence of anti-HAV IgM in the sample enables the HAV Viral Antigen and the Conjugate to bind to the solid phase. Excess Conjugate and HAV Viral Antigen are removed by a wash step, and a TMB Chromogen /Substrate solution is added to the microwells and allowed to incubate. If a sample contains anti-HAV IgM, the bound enzyme (HRP) causes the colorless tetramethylbenzidine (TMB) in the Chromogen solution to change to blue. The blue color turns yellow after the addition of a Stopping Solution. If a sample does not contain anti-HAV IgM, the Chromogen/Substrate solution in the well remains colorless during the substrate incubation, and after the addition of the Stopping Solution. The color intensity is measured spectrophotometrically. Absorbance value readings for patient specimens are compared to the cutoff value.

The performance of the MONOLISA™ Anti-HAV IgM EIA was evaluated in conjunction with the EVOLIS™ Automated Microplate System. The EVOLIS™ Automated Microplate System is a fully automated microplate analyzer that performs all functions necessary for the complete processing of microplate assays. Functions include: barcode scanning, sample

pre-dilutions, sample and reagent dispensing, plate incubations, plate wash cycles, photometric measurement of completed assay plates and results evaluation. The analyzer instrument is controlled via the EVOLIS™ software, a Windows® 2000 application running on a separate dedicated PC. An operator loads the appropriate microplates, assay reagents, and patient and control samples, then selects assay parameters, loads sample information, initiates instrument processing, and generates result reports.

5. Intended Use:

The MONOLISA™ Anti-HAV IgM EIA is an in vitro enzyme immunoassay kit intended for use in the qualitative detection of IgM antibodies to hepatitis A virus (anti-HAV IgM) in human (adult and pediatric) serum or plasma (EDTA, Heparin, Citrate, ACD). This assay is indicated for testing specimens from individuals who have signs and symptoms consistent with acute hepatitis. Assay results, in conjunction with other serological or clinical information, may be used for the laboratory diagnosis of individuals with acute or recent hepatitis A. The MONOLISA™ Anti-HAV IgM EIA is intended for manual use and with the Evolis™ Automated Microplate System in the detection of IgM antibodies to hepatitis A virus.

Assay performance characteristics have not been established for immunocompromised or immunosuppressed patients, and cord blood or neonatal specimens.

Warning: This assay is not intended for screening blood or solid or soft tissue donors.

6. Technological Characteristics

The following tables summarize similarities and differences between the MONOLISA™ Anti-HAV IgM EIA tested manually and the MONOLISA™ Anti-HAV IgM EIA tested with the EVOLIS™ Automated Microplate System.

Table 1: Similarities between devices

Parameter	MONOLISA™ Anti-HAV IgM EIA tested with the EVOLIS™ Automated Microplate System	MONOLISA™ Anti-HAV IgM EIA tested manually
Intended Use/Indications for Use	The MONOLISA™ Anti-HAV IgM EIA is an in vitro enzyme immunoassay kit intended for use in the qualitative detection of IgM antibodies to hepatitis A virus (anti-HAV IgM) in human (adult and pediatric) serum or plasma (EDTA, Heparin, Citrate, ACD).	The MONOLISA™ Anti-HAV IgM EIA is an in vitro enzyme immunoassay kit intended for use in the qualitative detection of IgM antibodies to hepatitis A virus (anti-HAV IgM) in human (adult and pediatric) serum or plasma (EDTA, Heparin, Citrate, ACD).
Assay procedure	Per the instructions in the package insert	Per the instructions in the package insert
Plate incubation	60 ± 5 minutes at 37°C + 2°C	60 ± 5 minutes at 37°C + 2°C
Plate washing	Wash with ≥ 370 µL of Working Wash Solution per well, and 30 - 60 second soak between each wash cycle for a total of 5 cycles.	Wash with ≥ 370 µL of Working Wash Solution per well, and 30 - 60 second soak between each wash cycle for a total of 5 cycles.
Result interpretation	Result interpretations, based on sample O.D.s, are determined according to package insert criteria.	Result interpretations, based on sample O.D.s, are determined according to package insert criteria.
Photometric measurement of completed assay plates	Read absorbance using 450 nm filter with 620 nm as the reference	Read absorbance using 450 nm filter with 615 to 630 nm as the reference

Table 2: Differences between devices

Parameter	MONOLISA™ Anti-HAV IgM EIA tested with the EVOLIS™ Automated Microplate System	MONOLISA™ Anti-HAV IgM EIA tested manually
Sample and reagent dispensing	Samples and reagents are dispensed by the automated system	Samples and reagents are dispensed manually
Barcode reading	Sample and reagent ID are verified automatically	NA or can be performed manually with barcode wand
Plate incubation	Plates are automatically moved to the incubation chamber	Plates are moved manually to the incubation chamber
Plate wash cycles	Plates are automatically washed	Plates are moved manually to an automated plate washer
Data management	Archives and retrieves data and sample information	NA
Spectrophotometric verification of sample and reagent pipeting	Performed automatically	Optional verification visually or with microplate reader

7. Performance Characteristics:

The performance of the MONOLISA™ Anti-HAV IgM EIA with the EVOLIS™ Automated Microplate System was compared to the MONOLISA™ Anti-HAV IgM EIA tested manually, which had previously received marketing clearance from the Agency. Substantial equivalence of the MONOLISA™ Anti-HAV IgM EIA, using manual equipment, was determined May 3, 2007 (k063319).

Correlation/method comparison

Studies have been performed with the MONOLISA™ Anti-HAV IgM EIA on the EVOLIS™ Automated System and compared to the results of testing the same kits and samples with the manual method. In this study 691 retrospective samples were tested on the MONOLISA™ Anti-HAV IgM assay using four (4) EVOLIS™ instruments at three sites. The same samples were tested manually (reference method) on the MONOLISA™ Anti-HAV IgM assay. The positive, negative and overall percent agreement along with the 95% confidence interval are presented below. In determining the percent agreement on borderline results, specimens that were borderline with the reference assay and negative with EVOLIS™ were considered as false negative for the EVOLIS™.

Table 2: MONOLISA™ Anti-HAV IgM EIA on EVOLIS™ vs. Manual Results

	EVOLIS™ Anti-HAV IgM Results			
Manual Anti-HAV IgM Results	**Reactive**	**Borderline**	**Nonreactive**	**Total**
Reactive	94	0	0	94
Borderline	1	0	0	1
Nonreactive	1	0	595	596
Total	96	0	595	691

The positive percent agreement with the reference method, manual testing, is 100% (94/94) with a 95% confidence interval of 96.1 – 100%. The negative percent agreement with the reference method is 99.7% (595/597) with a 95% confidence interval of 98.8 – 99.9%. The overall percent agreement is 99.7% (689/691) with a 95% confidence interval of 98.9 – 99.9%

The EVOLIS™ was also evaluated by performing a combination of 2 assays on the same plate. In this study 313 samples were tested with the MONOLISA™ Anti-HAV IgM EIA on a combination plate format on EVOLIS™ (two separate MONOLISA™ hepatitis assays run in a single microplate frame). Results were compared to the same samples tested manually (the reference method, individual plate format) on the MONOLISA™ Anti-HAV IgM assay. In determining the percent agreement on borderline results, specimens that were borderline with the reference assay (manual individual plate) and negative with EVOLIS™ (combination plate) were considered as false negative for the EVOLIS™ (combination plate).

Table 3: MONOLISA™ Anti-HAV IgM EIA on EVOLIS™ Combination Plate Testing vs. Manual Results

	EVOLIS™ Anti-HAV IgM Results Individual Plate			
Manual Anti-HAV IgM Results Combination Plate	**Reactive**	**Borderline**	**Nonreactive**	**Total**
Reactive	49	0	0	49
Borderline	1	0	0	1
Nonreactive	0	1	262	263
Total	50	1	262	313

The positive percent agreement with the reference method, manual testing, is 100% (49/49) with a 95% confidence interval of 92.7 – 100%. The negative percent agreement with the reference method is 99.2% (262/264) with a 95% confidence interval of 97.3 – 99.8%. The overall percent agreement is 99.4% (311/313) with a 95% confidence interval of 97.7 – 99.8%

Precision Study (Within-Laboratory)

A 21-member panel was tested: three (3) serum samples with six (6) corresponding plasma samples (EDTA K2, EDTA K3, Sodium Citrate, Sodium Heparin, Lithium Heparin, ACD) at three (3) different levels [1 low positive near the cutoff (Panel Set 1), 1 negative near the cutoff (Panel Set 2) and 1 negative (Panel Set 3)]. Two replicates each of the twenty-four (24) member panel were assayed twice a day for 20 days. The data were analyzed following the CLSI guidance EP5-A2, *Evaluation of Precision Performance of Quantitative Measurement Methods*. The mean ratio, the Standard Deviation (SD) and percent coefficient of variation (%CV) were calculated for each panel member.

The data summary is shown in the following tables, which summarize testing with the EVOLIS™ Automated System:

Table 4: MONOLISA™ Anti-HAV IgM EIA Precision Results by Panel Member Signal to Cutoff (S/CO)

Panel Member	N	Mean	Within run[1]		Between Run[2]		Between Day[3]		Total[4]	
		S/CO	SD	CV (%)	SD	CV (%)	SD	CV (%)	SD	CV (%)
Positive Control	80	1.97	0.035	1.8	0.091	4.6	0.163	8.3	0.190	9.7
High Negative	80	0.10	0.006	6.1	0.015	14.9	0.015	14.7	0.022	21.8
Cutoff Control	80	3.78	0.146	3.9	0.132	3.5	0.166	4.4	0.258	6.8
Serum (1)	80	1.55	0.036	2.3	0.076	4.9	0.138	8.9	0.161	10.4
EDTA K2 (1)	80	1.44	0.020	1.4	0.075	5.2	0.131	9.1	0.152	10.6
EDTA K3 (1)	80	1.49	0.030	2.0	0.083	5.6	0.126	8.5	0.154	10.3
Sodium Citrate (1)	80	1.48	0.033	2.2	0.086	5.8	0.140	9.5	0.168	11.3
Sodium Heparin (1)	80	1.41	0.024	1.7	0.080	5.7	0.132	9.4	0.156	11.1
Lithium Heparin (1)	80	1.39	0.026	1.9	0.077	5.5	0.120	8.7	0.145	10.5
ACD (1)	80	1.64	0.021	1.3	0.107	6.6	0.144	8.8	0.181	11.0
Serum (2)	80	0.62	0.016	2.7	0.031	5.0	0.059	9.5	0.068	11.1
EDTA K2 (2)	80	0.69	0.016	2.3	0.034	5.0	0.077	11.3	0.086	12.5
EDTA K3 (2)	80	0.69	0.014	2.0	0.046	6.6	0.073	10.5	0.087	12.5
Sodium Citrate (2)	80	0.74	0.014	1.9	0.044	5.9	0.075	10.1	0.088	11.9
Sodium Heparin (2)	80	0.66	0.011	1.6	0.041	6.2	0.061	9.2	0.074	11.2
Lithium Heparin (2)	80	0.66	0.020	3.0	0.040	6.1	0.058	8.9	0.073	11.1
ACD (2)	80	0.78	0.012	1.5	0.052	6.7	0.072	9.2	0.090	11.5
Serum (3)	80	0.10	0.004	3.6	0.010	9.7	0.010	10.1	0.015	14.5
EDTA K2 (3)	80	0.11	0.005	4.7	0.011	10.3	0.009	8.2	0.015	14.0
EDTA K3 (3)	80	0.10	0.004	4.2	0.010	9.5	0.011	10.6	0.015	14.8
Sodium Citrate (3)	80	0.10	0.003	2.9	0.009	9.2	0.010	9.8	0.014	13.8
Sodium Heparin (3)	80	0.10	0.004	3.8	0.009	8.7	0.010	9.9	0.014	13.7
Lithium Heparin (3)	80	0.10	0.015	4.5	0.010	9.5	0.010	9.2	0.014	14.0
ACD (3)	78	0.10	0.005	4.3	0.010	10.0	0.009	8.7	0.015	13.9

[1] Within Run: variability of the assay performance from replicate to replicate
[2] Between Run: variability of the assay performance from run to run
[3] Between Day: variability of the assay performance from day to day
[4] Total: total variability of the assay performance includes within run, between run and between day.

Reproducibility Study

A 6-member panel consisting of diluted plasma specimens (negative and different levels of positive) was tested in triplicate, once a day for 5 days with the MONOLISA™ Anti-HAV IgM EIA at 3 separate clinical trial sites. Each panel was coded with a different number on each day tested in order to blind the operator to the expected value of the sample. One (1) lot was used at each of 3 sites.

The data from all sites were combined to obtain standard deviation (SD) and percent coefficient of variation (CV) for within run, between day, between site and total variance. The data were analyzed according to the principles described in the Clinical Laboratory Standards Institute guidance EP15-A2, *User Protocol for Evaluation of Qualitative Test Performance*. The summaries are shown in the following tables:

Table 5: MONOLISA™ Anti-HAV IgM EIA Reproducibility Results by Panel Member Signal to Cutoff (S/CO)

Test Site	ID #	Panel Member	N	Mean (S/CO)	Within Run[1]		Between Day[2]		Total[3]	
					SD	%CV	SD	%CV	SD	%CV
Site #1	P1	Negative	30	0.16	0.033	20.5	0.014	9.0	0.036	22.4
	P2	High Negative	30	0.74	0.023	3.0	0.024	3.2	0.033	4.4
	P3	Low Positive	30	1.21	0.036	3.0	0.034	2.8	0.050	4.1
	P4	Low Positive	30	1.21	0.051	4.2	0.031	2.5	0.059	4.9
	P5	Positive	30	3.13	0.082	2.6	0.117	3.7	0.143	4.6
	P6	Positive	29	3.68	0.110	3.0	0.136	3.7	0.175	4.8
	P7	Positive Control	30	1.95	0.079	4.1	0.093	4.8	0.122	6.3
	P8	Negative Control	30	0.11	0.008	6.9	0.011	10.4	0.014	12.5
	P9	Cutoff Calibrator	30	3.28	0.139	4.2	0.159	4.9	0.211	6.4
Site #2	P1	Negative	30	0.17	0.013	7.7	0.008	5.0	0.016	9.2
	P2	High Negative	30	0.72	0.019	2.7	0.010	1.4	0.022	3.0
	P3	Low Positive	30	1.18	0.029	2.5	0.004	0.4	0.029	2.5
	P4	Low Positive	30	1.17	0.036	3.1	0.022	1.8	0.042	3.6
	P5	Positive	30	3.06	0.070	2.3	0.052	1.7	0.087	2.9
	P6	Positive	30	3.65	0.093	2.5	0.071	1.9	0.116	3.2
	P7	Positive Control	30	1.91	0.073	3.8	0.023	1.2	0.076	4.0
	P8	Negative Control	30	0.12	0.009	7.4	0.009	7.7	0.013	10.7
	P9	Cutoff Calibrator	30	3.54	0.245	6.9	0.118	3.3	0.272	7.7
Site #3	P1	Negative	30	0.16	0.015	9.0	0.021	13.0	0.025	15.8
	P2	High Negative	29	0.69	0.029	4.2	0.040	5.7	0.049	7.1
	P3	Low Positive	30	1.14	0.051	4.4	0.047	4.2	0.069	6.1
	P4	Low Positive	30	1.14	0.048	4.2	0.050	4.4	0.069	6.1
	P5	Positive	29	2.94	0.082	2.8	0.111	3.8	0.138	4.7
	P6	Positive	29	3.57	0.269	7.6	0.208	5.8	0.340	9.5
	P7	Positive Control	30	1.84	0.078	4.2	0.075	4.1	0.108	5.9
	P8	Negative Control	28	0.11	0.015	14.1	0.021	19.4	0.026	23.9
	P9	Cutoff Calibrator	28	3.56	0.278	7.8	0.343	9.6	0.441	12.4

[1] Within Run: variability of the assay performance from replicate to replicate
[2] Between Day: variability of the assay performance from day to day
[3] Total: total variability of the assay performance includes within run and between day

Table 6: MONOLISA™ Anti-HAV IgM EIA Reproducibility Summary by Panel Member Signal to Cutoff (S/CO)

Panel Member	N	Mean	Within Run[1]		Between Day[2]		Between Site[3]		Total[4]	
		S/CO	SD	%CV	SD	%CV	SD	%CV	SD	%CV
P1	90	0.16	0.022	13.5	0.014	8.9	0.000[5]	0.0	0.026	16.1
P2	89	0.72	0.024	3.3	0.027	3.8	0.021	2.9	0.042	5.8
P3	90	1.18	0.040	3.4	0.034	2.9	0.031	2.6	0.061	5.2
P4	90	1.17	0.045	3.9	0.036	3.1	0.032	2.8	0.066	5.7
P5	89	3.05	0.078	2.6	0.098	3.2	0.084	2.8	0.151	5.0
P6	88	3.63	0.176	4.8	0.144	4.0	0.000[5]	0.0	0.227	6.3
P7	90	1.90	0.077	4.0	0.070	3.7	0.044	2.3	0.113	5.9
P8	88	0.11	0.011	9.7	0.015	13.0	0.000[5]	0.0	0.018	16.2
P9	88	3.46	0.227	6.6	0.229	6.6	0.106	3.1	0.339	9.8

[1] Within Run: variability of the assay performance from replicate to replicate
[2] Between Day: variability of the assay performance from day to day
[3] Between Site: variability of the assay performance from site to site
[4] Total: total variability of the assay performance includes within run and between day, and between site
[5] Negative variances were rounded to zero, per statistical convention

Pipettor and washer carry-over

The pipette carryover study verified that the disposable tip pipettes on the EVOLIS™ do not carry residuals from one sample or well to another. In a washer carryover study, it was verified that the washer on the EVOLIS™ does not carry residuals from one well to another during the washing steps.

Pipetting accuracy

Dye studies were performed to determine pipetting accuracy for samples and reagents. These studies were conducted using 2 different volumes for samples and controls, and demonstrated pipetting accuracy with a CV of ≤7.7% across the microwell plate.

8. Conclusion

The MONOLISA™ Anti-HAV IgM EIA tested with the EVOLIS™ Automated Microplate System demonstrated equivalent performance to the MONOLISA™ Anti-HAV IgM EIA tested with the manual assay method, which had previously received FDA 510(k) clearance.

DEPARTMENT OF HEALTH & HUMAN SERVICES Public Health Service

Food and Drug Administration
10903 New Hampshire Avenue
Building 66
Silver Spring, MD 20993

Bio-Rad Laboratories
Attn: Linda Staswick
6565 185th Ave. NE
Redmond, WA 98052

OCT 29 2009

Re: K092353
Trade/Device Name: MONOLISA™ Anti-HAV IgM EIA with the EVOLIS™ Automated Microplate System
Regulation Number: 21 CFR 866.3310
Regulation Name: Hepatitis A virus (HAV) serological assays
Regulatory Class: Class II
Product Codes: LOL, JJE
Dated: July 30, 2009
Received: August 4, 2009

Dear Ms. Staswick:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration.

If your device is classified (see above) into class II (Special Controls), it may be subject to such additional controls. Existing major regulations affecting your device can be found in Title 21, Code of Federal Regulations (CFR), Parts 800 to 895. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21

CFR Part 807); labeling (21 CFR Parts 801 and 809); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803); and good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820). This letter will allow you to begin marketing your device as described in your Section 510(k) premarket notification. The FDA finding of substantial equivalence of your device to a legally marketed predicate device results in a classification for your device and thus, permits your device to proceed to the market.

If you desire specific advice for your device on our labeling regulation (21 CFR Parts 801 and 809), please contact the Office of *In Vitro* Diagnostic Device Evaluation and Safety at (301) 796-5450. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR Part 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to http://www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm for the CDRH's Office of Surveillance and Biometrics/Division of Postmarket Surveillance.

You may obtain other general information on your responsibilities under the Act from the Division of Small Manufacturers, International and Consumer Assistance at its toll-free number (800) 638-2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/cdrh/industry/support/index.html.

Sincerely yours,

Sally Hojvat, Ph.D.
Director
Division of Microbiology Devices
Office of In Vitro Diagnostics
Center for Devices and Radiological Health

Enclosure

Indications for Use

510(k) Number (if known): K092353

Device Name: MONOLISA™ Anti-HAV IgM EIA

Indication For Use:

The MONOLISA™ Anti-HAV IgM EIA is an in vitro enzyme immunoassay kit intended for use in the qualitative detection of IgM antibodies to hepatitis A virus (anti-HAV IgM) in human (adult and pediatric) serum or plasma (EDTA, Heparin, Citrate, ACD). This assay is indicated for testing specimens from individuals who have signs and symptoms consistent with acute hepatitis. Assay results, in conjunction with other serological or clinical information, may be used for the laboratory diagnosis of individuals with acute or recent hepatitis A. The MONOLISA™ Anti-HAV IgM EIA is intended for manual use and with the Evolis™ Automated Microplate System in the detection of IgM antibodies to hepatitis A virus.

Assay performance characteristics have not been established for immunocompromised or immunosuppressed patients, and cord blood or neonatal specimens.

Warning: This assay is not intended for screening blood or solid or soft tissue donors.

Prescription Use __X____ (21 CFR Part 801 Subpart D) And/Or Over the Counter Use ____. (21 CFR Part 801 Subpart C)

(PLEASE DO NOT WRITE BELOW THIS LINE; CONTINUE ON ANOTHER PAGE IF NEEDED)

Concurrence of CDRH, Office of In Vitro Diagnostic Device Evaluation and Safety (OIVD)

Uwe Schaf

Division Sign-Off
Office of In Vitro Diagnostic Device
Evaluation and Safety

510(k) K092353